

Appl. No. : 919,758
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AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph beginning on page 5, line 26 as follows:

In addition, molecules called PNA "clamps" have been synthesized which have two identical PNA sequences joined by a flexible hairpin linker containing three 8-amino-3,6-dioxaoctanoic acid units. When a PNA clamp is mixed with a complementary homopurine or homopyrimidine DNA target sequence, a PNA-DNA-PNA triplex hybrid can form which is extremely stable (Bentin et al., *Biochemistry* 35:8863-8869, 1996; Egholm et al., *Nucleic Acids Res.* 23:217-222, 1995; Griffith et al., *J. Am. Chem. Soc.* 117:831-832, 1995). The sequence-specific and high affinity duplex and triplex binding of PNA have been extensively described (Nielsen et al., *Science* 254:1497-1500, 1991; Egholm et al., *J. Am. Chem. Soc.* 114:9677-9678, 1992; Egholm et al., *Nature* 365:566-568, 1993; Almarsson et al., *Proc. Natl. Acad. Sci. U. S. A.* 90:9542-9546, 1993; Demidov et al., *Proc. Natl. Acad. Sci. U. S. A.* 92:2637-2641, 1995). They have also been shown to be resistant to nuclease and protease digestion (Demidov et al., *Biochem. Pharm.* 48:1310-1313, 1994). ~~DNA analogs such as phosphorothioates are also contemplated herein (see U.S. Patent No. 5,459,127).~~

Please amend the paragraph beginning on page 8, line 26 bridging to page 9 as follows:

Although any transfection method well known in the art may be used to transfect the transcriptionally active PCR fragments of the invention into cells or tissues including calcium phosphate precipitation, electroporation and DEAE-dextran, cationic lipid-mediated transfection is preferred. Gene delivery systems are described by Felgner et al. (*Hum. Gene Ther.* 8:511-512, 1997) and include cationic lipid-based delivery systems (lipoplex), polycation-based delivery systems (polyplex) and a combination thereof (lipopolyplex). Cationic lipids are described in U.S. Patent Nos. 4,897,355 and 5,459,127, the entire contents of which are hereby incorporated by reference. As set forth in U.S. Patent No. 5,459,127, "[p]articularly preferred contemplated uses of the invention are deliveries of either an antisense polynucleotide or ribozyme as described above, and having as its target the rev site of the HIV genome (Scientific American, October, 1988, pp. 56-57). Matsukura, M. et al. Proc. Nat'l. Acad. Sci. 86:4244-4248 (1989) describe a 28-mer phosphorothioate compound anti-HIV (anti-rev trans activator) specific for the site. Other therapeutic uses of cationic lipids herein disclosed include: the liposomal delivery of nucleoside

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or nucleotide analogues having an antiviral effect, such as dideoxynucleotides, didehydronucleotides, nucleoside or nucleotide analogues having halo-substituted purine or pyrimidine rings such as 5-trifluoromethyl-2'-deoxyuridine or 5-fluorouracil; nucleoside or nucleotide analogues having halo- and azido-substituted ribose moieties, such as 3'-azido-3'-deoxythymidine (AZT), nucleoside analogues having carbon substituted for oxygen in the ribose moiety (carbocyclic nucleosides), or nucleotide analogues having an acyclic pentose such as acyclovir or gancyclovir (DHPG). The liposomal delivery of such analogues is disclosed in U.S. patent application Ser. No. 099,755 filed September, 1987 by Hostetler and Richman. The antiviral potency of these analogues is found to be increased when they are presented to the cells as phospholipid derivatives. These derivatives may be incorporated into the liposomal structure for administration to cells thereby forming a more stable liposomal complex which can deliver greater amounts of drugs to target cells with less toxicity. Effective antiviral lipid derivatives of nucleoside analogues comprise phosphatidyl 2',3'-dideoxynucleosides, 2',3'-didehydronucleosides, 3'-azido-2'-dideoxynucleosides, 3'-fluorodeoxynucleosides and 3'-fluorodideoxynucleosides, 9-beta.-D-arabinofuranosyladenine (araA), 1-beta.-D-arabinofuranosylcytidine (araC), nucleosides such as acyclovir and gancyclovir having an acyclic ribose group, or the same nucleoside analogues as diphosphate diglyceride derivatives. Preferred species of lipid derivatives of antiviral or antiretroviral nucleoside analogues for the treatment of HIV infection using cationic lipid mediated liposomal delivery are phospholipid derivatives of 3'-azido-2',3'-dideoxypyrimidine, 3'-halopyrimidine dideoxynucleoside, or a 2',3'-didehydro-2',3'-dideoxynucleoside, for example, phosphatidyl 3'-azido-3'-deoxythymidine (pAZT) or phosphatidyl 2-chlorodeoxyadenosine. Certain viral infections, comprising herpes, cytomegalovirus, and hepatitis B infections are effectively treated with nucleoside analogues comprising acyclovir, gancyclovir, 1-(2'-deoxy-2'-fluoro-1-beta.-D-arabinofuranosyl)-5-iodocytosine (FIAC) or 1-(2'-deoxy-2'-fluoro-1-beta.-D-arabinofuranosyl)5-iodouracil (FIAU). Phospholipid derivatives of these agents, preferably the phosphatidyl and diphosphate diglyceride derivatives can be administered in these diseases using cationic lipid liposomal delivery systems, according to the invention. Details of the structures, synthesis and liposomal delivery of lipid derivatives of antiviral nucleosides are presented in U.S. patent applications Ser. Nos. 216,412; 319,485; and 373,088 which are hereby incorporated by reference."